

Outcome in cardiac surgery

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Valorisation

Cardiovascular disease (CVD) is the leading cause of mortality for women in Europe (49% in women and 40% in men). There is still an ongoing misperception that women under the age of 65 years are at low risk for CVD. Even medical practitioners are prone to the misconception of CVD being a predominantly male problem. Women undergoing coronary artery bypass grafting (CABG) have a different perioperative risk profile compared to men and their postoperative outcome is worse. It is still not completely understood which factors contribute to women having a worse outcome compared to men. Both in the EuroSCORE as well as in the STS score who are used to estimate the risk of perioperative mortality in cardiac surgery, the 'risk factor' female gender gives a higher change of mortality compared to male gender.

It was our main goal to study perioperative risk factors in relation to the 'risk factor' female gender. The department of cardiac thoracic surgery of the Catharina Hospital has an extensive database which has been maintained from 1998 until now. That is why we can conduct extensive research into large groups of patients and draw statistically significant conclusions.

The first study we performed is described in Chapter 2: a large cohort of patients (13,903 men and 4,016 women) was studied. The main finding was the considerable difference in preoperative profile between male and female populations undergoing CABG. Women were older than men at the time of CABG and had greater number of preoperative comorbidities, including hypertension, diabetes, obesity, and anemia. Probably, women experience a delayed onset of cardiac disease, compared to men, until the onset of menopause, presumably because of the protective effects of estrogen on the cardiovascular system. The incidence of early mortality was significantly higher in women than in men (2.7% versus 1.9% $p=0.001$) and the predictive value of well-known risk factors for early mortality was different between the 2 sexes. Chronic obstructive pulmonary disease (COPD), peripheral vessel disease (PVD) and underweight were identified as independent risk factors for early mortality only in men. These findings must be considered when stratifying the risk for CABG patients.

Differences between men and women in long term outcome, mean follow-up period was 9.6 ± 4.9 years, after CABG is described in Chapter 3. Here we reviewed all consecutive patients (total 17,663) undergoing CABG and after statistical analysis early mortality and 1-year mortality were significantly higher in women compared to men. Also, women showed a worse overall long-term survival than men. Multivariate analysis revealed female sex, age, hypertension, diabetes, PVD, COPD, prior cerebral vascular accident (CVA), left ventricular dysfunction as significantly associated with higher long-term mortality. We

also performed propensity score-matched analyses (3,926 man and 3,926 women) and analyzed the independent risk factors for short-, medium- and long-term mortality. The main conclusion of the outcome of this propensity matched group was that female sex was not an independent risk factor for long-term mortality. It seems logical that independent risk factors, and not female gender, predicts the outcome in survival after CABG. Therefore female gender must be excluded as a risk factor for long-term mortality.

Off pump coronary artery bypass grafting (OPCAB), used for the first time in the nineties, is still a well-established technique for treatment of CVD. Several authors reported about the advantages and disadvantages of OPCAB since this technique was introduced. There are some studies which showed that women might have better survival after OPCAB surgery compared to on-pump coronary artery bypass grafting (ONCAB). In Chapter 4 we compared two groups of patients in outcome after CABG, OPCAB versus ONCAB. The 120-days mortality showed that the OPCAB female group has three times lower mortality than the ONCAB female group (1.2% versus 3.6%). This is an important finding, OPCAB surgery is the preferential treatment for women suffering from CVD.

Aortic valve replacement (AVR) is a common surgical procedure in our cardiac thoracic surgery practice. As people become older, there is a growing population of patients undergoing AVR. In Chapter 5 we compared patient profiles and outcomes of men and women undergoing isolated aortic valve replacement. In a nineteen year period we evaluated 2362 patients, 1040 (44%) of whom were women and 1322 were men (56%). Although women have relatively more risk factors than men, like older age (69.9 years vs. 64.6 years, $p<0.001$), more underweight, obese and diabetic. They also had lower hemoglobin and worse renal function than men but less women suffered from chronic obstructive pulmonary disease, aortic regurgitation, left ventricular dysfunction and endocarditis than men. Early mortality in women was not significantly higher than in men, but the overall survival was worse in women than in men. After adjustment for preoperative risk factors, there is no difference in overall survival between women and men. The estimated mortality risk score, used by cardiologists and cardiac surgeons, is the EuroSCORE where female gender is a predictor of higher mortality. In our study the risk factor 'female gender' had no influence on the overall survival in patients undergoing AVR, this should be further investigated.

Unfortunately transfusion of blood products after CABG is associated with increased morbidity and mortality. Because we have built up a large detailed database over the last 20 years, it was possible to study the results of a large cohort of patients undergoing CABG and the use of blood products in relation to mortality, as discussed in Chapter 6. We included 18,992 patients who underwent isolated CABG, between 1998 and 2017. In time, the rates of perioperative RBC transfusion decreased for all patients undergoing isolated CABG (52.1% in 1998 versus 18.6% in 2017). The mean number of transfused RBC

units was significantly higher in females compared to males (1.57 ± 2.2 versus 0.68 ± 1.84 ; $p < 0.005$) and after adjusting the results for other risk factors, female sex was a significant independent factor for perioperative RBC transfusion. If we can change the guidelines for prescribing RBC, not only the costs associated with consuming RBC will drop significantly, also mortality after CABG will decline especially in women.

To conclude, women have another risk profile for cardiac surgery compared to men and therefore a worse outcome in mortality, preoperative risk factors predicts the outcome after CABG and not female gender. OPCAB is a better operation technique than CABG for women suffering CVD. Mortality after AVR is estimated by using the EuroSCORE, female gender may no longer need to be considered as a risk factor. Female gender is a significant independent risk factor for perioperative RBC transfusion.